UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/722,467	11/28/2003	Philippe Du Mesnil	P63187US2	7970

136 7590 08/17/2007

JACOBSON HOLMAN PLLC
400 SEVENTH STREET N.W.
SUITE 600
WASHINGTON, DC 20004

EXAMINER	
WILLIAMS, LEONARD M	
ART UNIT	**PAPER NUMBER**
1617	

MAIL DATE	DELIVERY MODE
08/17/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/722,467	DU MESNIL ET AL.	
	Examiner	Art Unit	
	Leonard M. Williams	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 12-20 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 12-20 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

Response to Arguments

Applicant's arguments filed 05/29/2007 have been fully considered but they are not persuasive. No amendments were made to the claims.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

The applicant's have argued on pages 6-7 of the remarks that Siris is drawn only to treatment of Paget's disease and while admitting that Paget's disease is associated with osteoarthritis assert that Siris is drawn only to, at best, prevention of osteoarthritis and/or Paget's disease and not treatment or even concurrent treatment of Pagets'

disease and osteoarthritis. This position is untenable. It is not a necessary cause that osteoarthritis must be present in order for Paget's disease to be present or vice-versa for the prior art to be inherently treating an overlapping patient population and/or condition. The reference clearly shows a link between Paget's disease, osteoarthritis and the treatment of such patients with the claimed compounds (or closely related bisphosphonates). If the compounds administered for Paget's disease in a patient suffering from osteoartthritis and/or lameness, happen to treat the osteoarthritis and/or lameness due to their inherent biological activities, the initial reasons for their administration are irrelevant.

For the reasons stated above and for the reasons of record all rejections from the previous office action are maintained and reproduced below.

This action is made **final**.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 12-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Biere et al. (US Patent No. 4473560), in view of Barbier et al. (US Patent No. 5488041) and further in view of Siris (A Potent New Bisphosphonate for Paget's Disease of Bone, 1996, The American Journal of medicine, vol. 101, pp. 339-340).

Biere et al. teach, in col. 1 line 10 to col. 2 line 28, diphosphonic acid derivatives of formula I possessing pronounced antiinflammatory and antiarthritic activity. Further they affect the productive and destructive power of osteoblasts and osteoclasts. The antiarithric activity of the compounds can be used for therapy of rheumatoid arthritis,

osteoarthritis, ankylosing spodylitis and other related diseases of the collagen and the skeletal system (osteoporosis and Paget's disease). The compounds can be employed as full esters or di-monoesters, but preferably are utilized as free phosphonic acids and/or their physiologically compatible salts such as Na, K, Ca, Ba, Sr, Mg etc... The compounds can be formulated for enteral or parenteral administration including capsules, tablets, dragees, suppositories, and injection and dermal applications. The compounds can be administered at doses of 1-50mg/kg/day orally.

Biere et al. does not teach the particularly claimed diphosphonic acid derivatives, nor the use of the diphosphonic acid derivatives on animals of the equidae family, nor the intravenous administration of from 0.1-1 mg/kg/week of tiludronic acid to horses, nor directly the treatment of lameness caused by osteoarthritis.

Barbier et al. teach, in the abstract and in col. 3 lines 10-35, a method of promoting bone repair in human or veterinary medicine which comprises the administration of a therapeutically effective amount of bisphosphonic acid derivatives (see Formula I). Said method is particularly suitable following a fracture or bone surgery. It includes the use of drugs containing at least one bisphosphonic acid derivative.

Such drugs can be used in human medicine and in veterinary medicine.

Such drugs can be administered by different modes of administration, for example orally, parenterally, transdermally or by means of an implant.

When a drug for oral administration is prepared, it is possible to use any suitable excipient and in particular an excipient which facilitates the absorption of the drug, such as sodium laurylsulfate.

The administration doses of the drug according to the invention depend on the bisphosphonic acid derivative used, the mode of administration and the magnitude of the desired effect on bone repair.

The drug administered according to the invention can be administered as a single or repeat dose. For repeat-dose administration, it is possible to choose daily continuous administration, 1 to 3 times a day, throughout the duration of the fracture repair (one to several months), or intermittent administration, for example 1 day a week for one to several months.

The dosage unit can comprise from 0.001 mg to 400 mg of bisphosphonic acid derivative(s) of formula (I), more particularly 0.01 mg to 400 mg.

Thus the administration doses of the drug prepared according to the invention can vary from 0.001 mg to 1.2 g per day, more particularly from 0.01 mg to 1.2 g per day.

The dosage unit preferably comprises from 0.1 to 250 mg of bisphosphonic acid derivative(s) of formula (I).

Barbier et al. teach in column 1 line 25 to col. 2 line 30, that the preferred bisphosphonates of formula I include etidronic acid, piridronic acid, clodronic acid, pamidronic acid, alendronic acid, phenoxymethylenebisphosphonic acid, tiludronic acid, risedronic acid, 1-hydroxy-2(imidazol-2-yl)ethyl-1,1-bisphosphonic acid and 2-

hydroxythylidene-2-(pyridin-3-yl)-1,1-bisphosphonic acid and their respective pharmaceutically acceptable salts (all being bisphosphonic acid derivatives detailed in applicant's claim 12).

Barbier et al. teach in col. 2 lines 44-49, that several of the bisphosphonic acid derivatives are being studied for use in the treatment of bone diseases such as Paget's disease and osteoporosis.

Siris teaches on pages 339-340, that Paget's disease is a localized disorder of bone remodeling. The disease causes formation of increased numbers of greatly enlarged osteoclats at localized sites. These changes predispose to bone deformity and fracture. Depending on the location of the affected bones and the severity of the level of abnormal bone remodeling, Paget's disease may be asymptomatic or may induce a variety of symptoms including bone pain, osteoarthritis at adjacent joints, deformity, neurological compression and fracture of the vertebrae or extremities. Effective treatments for Paget's diseases include the intravenous use of pamidronate (a bisphosphonic acid derivative), oral administraion of alendronate (a bisphophonic acid derivative), and etidronate (a bisphosphonic acid derivative). The bisphosphonic acid derivates are capable of restoring the pagetic increase in bone remodeling in a large majority of patients, in addition to providing relief of those symptoms likely to respond to a reduction in bone turnover.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the compounds of Barbier et al. in the treatment of lameness caused by osteoathritis (in horses) as Biere et al. teaches that the antiarithric activity of

the biphosphonic acid derivatives is useful for the therapy of rheumatoid arthritis, ***osteoarthritis***, ankylosing spodylitis and other related diseases of the collagen and the skeletal system (osteoporosis and ***Paget's disease***), further Barbier et al. disclose the currently claimed compositions as suitable for vet nary use (thus encompassing horses) and Siris teaches that Paget's disease can induce osteoarthritis, causes localized bone pain (which is one source of lameness) and is treatable with the currently claimed compounds.

The examiner respectfully points out the following from MPEP § 2112.01: "[T]he discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." Atlas Powder Co. v. Ireco Inc., 190 F.3d 1342, 1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). Thus the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. In re Best, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977).

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leonard M. Williams whose telephone number is 571-272-0685. The examiner can normally be reached on MF 9-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

LMW

SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER